Chloroacetic acid induced cell apoptosis through ROS/endoplasmic reticulum stress pathway in neuronal cell

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Abstract:

Chloroacetic acid (CA), a toxic chlorinated analog of acetic acid, is widely used as an herbicide and in the synthesis of many organic compounds. Some studies have reported that CA can cause histopathological alterations and functional impairment in brain. However, the toxicological effects and underlying mechanisms of CA-induced neurotoxicity are mostly unclear. Here, we investigated the effects and possible mechanisms of CA in cultured neuron cells (Neuro-2a cells). Treatment of Neuro-2a cells with CA for 24h significantly induced cytotoxicity, reduced cell viability, and oxidative stress damage (membrane LPO production) which accompanied by several

features of apoptosis, including the increases in Annexin V-binding cells and caspase-3/-7 activity. CA also triggered endoplasmic reticulum (ER) stress as indicated by the enhancement in ER stress-related mRNA and protein molecules induction (such as glucose-regulated protein 78 (GRP78), GRP94, C/EBP homologue protein (CHOP), X-box binding protein 1 (XBP-1)), procaspase-12 cleavage, and calpain activation. Transfection of cells with GRP78 or GRP94 siRNA reduced CA-induced caspase-3 expression in Neuro-2a cells. Meanwhile, these CA-induced apoptosis and ER stress-related signals could be effectively reversed by antioxidant *N*-acetylcysteine (NAC). Therefore, our results suggest that CA caused neuron cell apoptosis via oxidative stress-triggered ER stress signaling pathway.

Keywords: Chloroacetic acid; Neurotoxicity; apoptosis; Oxidative stress; ER stress